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Microwave Assisted Synthesis, Spectroscopic Characterization and Antimicrobial Activities of Co(II) Complexes Containing Biologically Active Thiosemicarbazone Derivatives

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Abstract In present study two thiosemicarbazone ligands i.e. 4HAT and 3NBT and their novel Cobal(II) aryl thiosemicarbazones complexes having the general composition $[Co(L_1)_2Cl_2]$, $[Co(L_2)_2Cl_2]$,{where L_1= 4-Hydroxyacetophenone thiosemicarbazones (4HAT), L_2 = 3-Nitrobenzaldehyde thiosemicarbazones (3NBT), have been synthesized by the reaction of thiosemicarbazide with substituted aromatic aldehydes and ketones by conventional heating as well as microwave irradiations method followed by complexation with Cobalt(II) metal. The synthesized compounds have been characterised by elemental analysis, melting point determination, FTIR, UV-visible spectral analysis. The synthesized ligands and their new metal complexes have been screened in vitro for antibacterial activity against *Escherichia coli*, *Staphylococcus aureus* and *Bascillus subtilis* bacteria.

Keywords Thiosemicarbazones, Microwave irradiation, Cobalt(II) complexes

1. Introduction

Thiosemicarbazones is an important class of compounds obtained by condensing thiosemicarbazide with suitable aldehydes or ketones [1]. The active group for chelation is Sulphur [2]. In most of the complexes, the thiosemicarbazones coordinate to the metal ion as a bidentate ligand bonding through the sulphur atom and the hydrazino nitrogen atom. In a few cases they behave as unidentate ligands by bonding only through the sulphur atom. In certain cases thiosemicarbazones also act as multidentate ligands if donor groups are also present in the parent aldehyde or ketone moiety [3]. Transition metal complexes with N,N- and N,S-donor ligands have attracted remarkable attention because of their interesting chemical and biological properties [4]. It is well known that N and S atoms play important roles in the coordination of metal ions at active sites of numerous metallobiomolecules [5]. Interest in metal complexes with thiosemicabazone ligands has been stimulated because biological activities are often enhanced on complexation [6]. Thiosemicarbazones and their metal complexes have received considerable attention because of their antibacterial, antifungal, antitumor, antiamoebic, antimalarial, antiviral, radioprotective, trypanocidal and anti-inflammatory activities [7-22]. With the growing interest of thiosemicarbazones the present work was undertaken in order to investigate the ligational behaviour of the thiosemicarbazone towards Co(II) metal ion as well as their biological activity in inhibiting the growth of some pathogenic bacteria [23].

Materials and methods

All the chemicals and solvents used were of AR grade and procured from Sigma-Aldrich and E Merck and used as received. Purity of synthesized compounds has been checked by thin layer chromatography. IR spectra are recorded on Bruker Optic Model Alpha (FT-IR) (Zn-Se Optics, ATR) (4000-500 cm-1) using KBr disc. Magnetic susceptibility measurements were carried out on the vibrating sample magnetometer (VSM) model 155 at 5500 Gauss field strength. Microwave synthesis was carried out in domestic microwave oven Model KENSTAR-OM20ACF, 2450MHz, 800W and GMBR (Green Microwave Biochemical Reactor) at GCRC, P.G. Dept. of Chemistry, Govt. Dungar College (NAAC-A- Grade) MGS University Bikaner, Rajasthan. ECIL Double Beam UV-Visible Spectrophotometer, model UV 5704SS, with quartz cell of 10 mm light path was used for absorption measurement. All biological activities have been carried out with horizontal laminar at BIFR, Bikaner.

Preparation of Ligand

Microwave irradiation synthesis of ligands

Two ligands *i.e.* L_1= 4-Hydroxyacetophenone thiosemicarbazone (4HAT), L_2 = 3-Nitrobenzaldehyde thiosemicarbazone (3NBT), were synthesized. In a typical preparation water or water alcohol mixture of thiosemicarbazide (0.01mol) and aldehyde or ketone (0.01mol) were taken in Erlen Meyer flask capped with a funnel placed in a microwave oven and irradiated at 200 watt for 2-5 minutes. The reaction was monitored by TLC. After completion the reaction, the reaction mixture was allowed to attain room temperature and solid separated was filtered. The crude product was recrystallized from redistilled ethanol.

Thermal method

For comparison purposes, the above ligands were also synthesized by the thermal method, where instead of a few drops of alcohol, a hot ethanolic solution (25 mL) of aldehyde or ketone (0.01 mol) was mixed to a hot ethanolic refluxing solution (30 mL) of thiosemicarbazide (0.01 mol) in a 1 : 1 molar ratio. The contents were refluxed for about 6-10 hours in a water bath. The solution was then concentrated under reduced pressure, which upon cooling gave crystalline precipitates. The products were washed in alcohol and recrystallized in the same solvent. The structures of ligands are shown in (Fig. 1). A comparison between the thermal method and microwave method is given in (Table 1).

Preparation of the complexes

Two different methods were employed for the synthesis of the metal complexes with each of the ligands. A comparison between the thermal method and microwave method has been given in Table 1.

Microwave method

For the preparation of complexes, a slurry of ligands (i.e. 4HAT, 3NBT,) (0.2mmol) was prepared in water or in water-ethanol mixture. In this, solution of Cobalt Chloride (0.01mm in 30 ml ethanol) was added. The resulting mixture was irradiated in a microwave oven for 2 to 6 minutes at medium power level (600W) maintaining the occasional shaking. The mixture was cooled to room temperature and poured into ice chilled methanol and dried in vacuum over P_2O_5 [24].

Thermal method

The complexes were also synthesized by the thermal method. In this method hot ethanolic solution (20ml) of the corresponding ligand (0.02mmol) and hot ethanolic solution (20ml) of the $CoCl_2.6H_2O$ (0.01mmol) were mixed with constant stirring. The reaction mixture was refluxed after adding 4-5 drops of glacial acetic acid for 8-10 hours at 80-90° C. On cooling colored complexes were precipitated out. They were filtered, washed with 50% ethanol and dried in vacuum desiccators and recrystalized in ethanol. The obtained solid metal complexes and their colors are shown in table 1.

Results and discussion

Ligands and complexes were identified on the basis of elemental analysis and spectral studies. Colour, yield and elemental analysis data are represented in Table 1.

Infrared Spectra

The binding mode of the ligand to metal ions was further elucidated by analysis of the IR spectra of the ligands and metal colmplexes (table 2). A study and comparison of infrared spectra of free ligand and its metal complexes imply that the ligand behaves as bidentate and the metal ion is coordinated through the azomethine nitrogen and the thione sulphur. A band in the range 1660 - 1600 cm^{-1} in the IR spectra of the ligands is due to *v*(C=N) [25]. Coordination of azomethine nitrogen in complexes is suggested by the shift of *v* (C=N) band to lower frequencies. The absence of a *v*(S-H) absorption in the region 2700-2500 cm^{-1} is considered as evidence that the thione form of the ligands exist in the solid state [26-27]. The intensity of the medium band in the range 1100 – 1060 cm^{-1} assigned for *v* (N-N) in spectrum of the ligands is remains unchanged in all the spectra of the complexes, however, it shifted to the higher frequency. The strong band observed in the range 880 - 820 cm^{-1} assigned for *v*(C=S) in spectrum of the ligands is shifted towards lower frequency and occurred at 860 - 805 cm^{-1} in the corresponding spectra of the metal complexes indicating the coordination of the thione sulphur to metal atom[28-29]. The bands in the range 3200 - 3140 cm^{-1} in ligands are due to NH vibration. In all the complexes, the presence of a band in this region corresponds to NH vibration which indicates that the ligand is coordinated in the neutral form.

Magnetic Moments and Electronic Spectra

The observed magnetic moments at room temperature of Co(II) complexes fall in the range 4.85 – 5.18 BM. These values are typical of distorted octahedral geometry coordinated around Cobalt which has three unpaired electrons. The electronic spectra of these complexes have been recorded in DMF are reported in table 3. The electronic spectra of all the Co(II) complexes recorded were very similar to each other and consist of two bands in the regions 18868 - 18132 cm^{-1} and 20876-19666 cm^{-1}, which clearly indicated the octahedral stereochemistry of the complexes. The band maxima and their assignments are presented in Table 3.

Biological activity

The antibacterial activity of the compounds against *E.coli*, *S.aureus* and *B.subtilis* were carried out using Muller Hinton Agar media (Hi media). The activity was carried out using paper disc method is represented in Table 4 which shows all the Cobalt(II) complexes have moderate antibacterial activities against these bacteria. Ligands 4HAT, 3NBT and their Co(II) Complexes has been found out to be effective against these bacteria showing maximum clarity of zones.

Conclusion

The thiosemicarbazone ligand and its Co(II) complexes were characterized by elemental analysis, spectral studies and magnetic moment measurements. On the basis of above data the thisemicarbazone ligands appear to behave as bidentate ligand coordinating through the azomethine nitrogen and the thione sulphur atom. The results of the above studies suggest that the Co(II) complexes probably possess a distorted octahedral geometry. The antibacterial properties of the ligands and its complexes were studied against *E.coli*, *S.aureus* and *B.subtilis* bacteria. The result shows that all the Cobalt(II) complexes have moderate antibacterial activities against these bacteria.

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Table 1: Physico-Chemical Data of Ligands and their Co(II) complexes(C.M. = conventional method, M.M. = Microwave method)

S. No.	Compound	Colour	Reaction period		Yield %		Elemental Analysis Calcd (Found) %		
			CM (Hrs.)	MM (Min.)	CM	MM	C	H	N
1	4HAT	Yellow	6	4.5	61	74	45.38 (45.19)	4.20 (4.08)	23.53 (23.59)
2	3NBT	Light Brown	6.5	4	62	69	42.86 (42.77)	3.58 (3.49)	25.00 (25.12)
5	$[Co\text{-}(4HAT)_2Cl_2]$	Z-Black	6.5	3.00	52	63	39.21 (39.29)	4.02 (4.27)	15.33 (15.19)
6	$[Co(3NBT)_2]Cl_2$	Light Brown	6	4.5	52	64	33.22 (33.14)	2.77 (2.64)	19.38 (19.28)

Table 2: Significant infrared spectral bands (cm^{-1}) of the ligands and its metal complexes

Compounds	*ν*(C=N)	*ν*(N-N)	*ν*(C=S)	*ν*(N-H)	*ν*(M-N)	*ν*(M-S)
4HAT	1654	1078	830	3198	-	-
3NBT	1660	1067	818	3157	-	-
$[Co(4HAT)_2]Cl_2$	1564	1177	819	3228	479	444
$[Co(3NBT)_2]Cl_2$	1604	1067	817	3157	449	433

Table 3: Magnetic moments and electronic spectral data of Co(II) complexes

S. N.	Complex	μ_{eff} (BM)	Electronic Spectral bands $\lambda_{max}(cm^{-1})$	Tentative assignments	Comments
1	Co(II)-4HAT	5.15	20020,18066,	$^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$	Distorted octahedral Co(II) Geometry
2	Co(II)-3NBT	4.98	18320,20450	$^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$	Distorted octahedral Co(II) Geometry

Table 4: Antibacterial activity of synthesized compounds

S. N.	Compounds (100ppm)		Zone of inhibition (in mm)		
			E. coli	*S. aureus*	*B. subtilis*
1	4HAT		1.0	3.0	0.5
2	3NBT		0.5	1.0	0.5
5	$[Co(4HAT)_2]Cl_2$	1.0	1.0	0.5	
6	$[Co(3NBT)_2]Cl_2$	0.5	0.5	0.5	

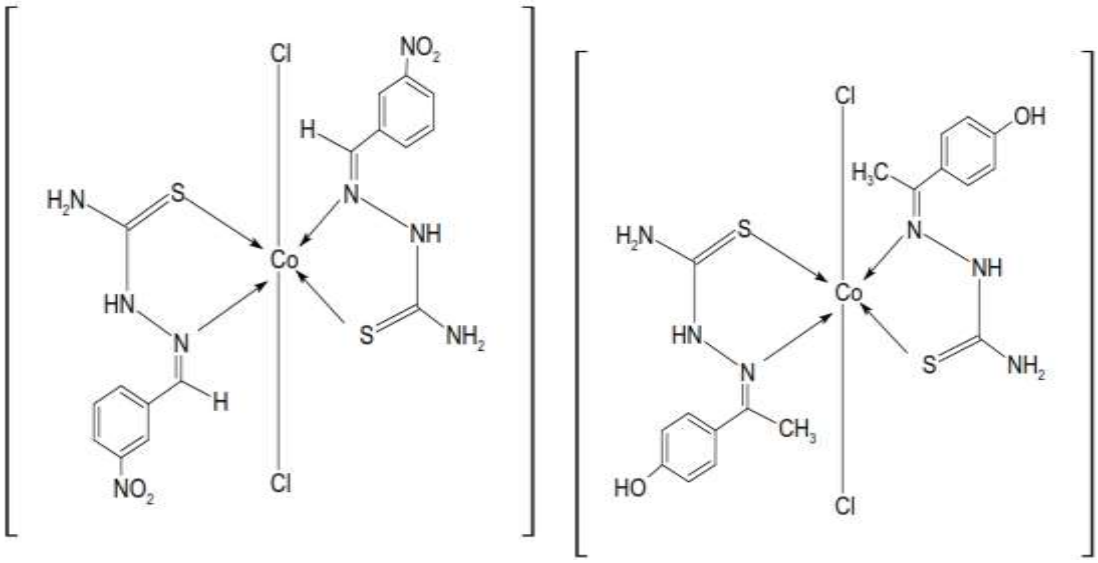

Figure 2: Tentative Structures of Co(II) Complexes

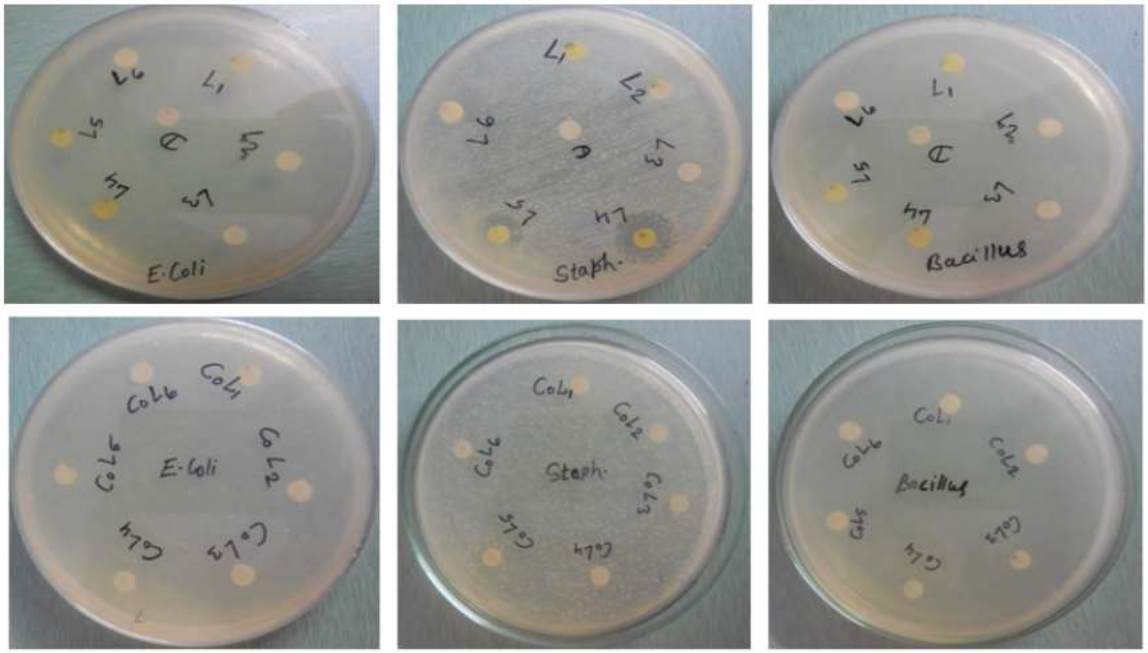

Figure 3: Antibacterial activity

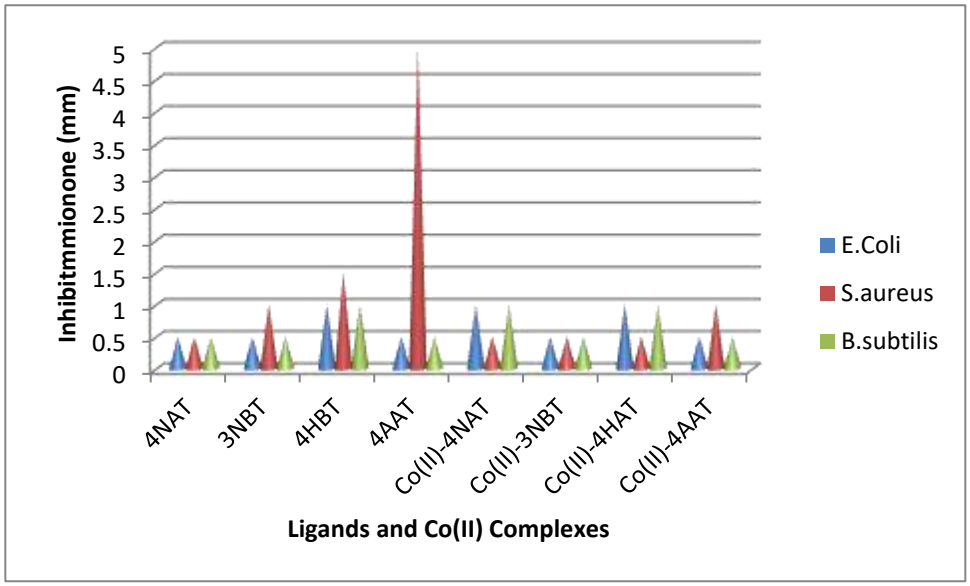

Figure 4: Graphical Presentation of Biological Activity

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